UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/826,319	04/03/2001	Michael F. Lahn	2879-80	4155

22442 7590 04/06/2007

SHERIDAN ROSS PC
1560 BROADWAY
SUITE 1200
DENVER, CO 80202

EXAMINER	
SCHWADRON, RONALD B	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/826,319	LAHN ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32 and 34-36* is/are pending in the application.

4a) Of the above claim(s) *3-8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,9-32,34-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. In view of the Brief filed on 11/20/06, PROSECUTION IS HEREBY REOPENED. As set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below.

2. Claims 1,2,9-32,34-36 are under consideration.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1,2,9-32,34-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). In the instant case, the specification

does not convey to the artisan that the applicant had possession at the time of invention of the claimed inventions.

The claims encompass use of antibodies which bind TCR or CD3 or CD4 or CD8 from any mammal. Thus the claims encompass use of antibodies which bind the aforementioned molecules from any of the thousands of mammalian species. Whilst the murine and human counterparts of the aformentioned molecules derived from mouse or humans were known in the art, there are thousands of mammalian species wherein said molecules have not been isolated or characterized at the amino acid sequence level. The skilled artisan cannot envision the detailed structure of the encompassed antibodies and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. In the instant application, the peptide itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

In view of the aforementioned problems regarding description of the claimed invention, the specification does not provide an adequate written description of the invention claimed herein. See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1404-7 (Fed. Cir. 1997). In University of California v. Eli Lilly and Co., 39 U.S.P.Q.2d 1225 (Fed. Cir. 1995) the inventors claimed a genus of DNA species encoding insulin in different vertebrates or mammals, but had only described a single species of cDNA which encoded rat insulin. The court held that only the nucleic acids species described in the specification (i.e. nucleic acids encoding rat insulin) met the description requirement and that the inventors were not entitled to a claim encompassing a genus of nucleic acids encoding insulin from other vertebrates, mammals or humans, id. at 1240. The Federal Circuit has held that if an inventor is "unable to envision the detailed constitution of a gene so as to distinguish it from other materials. . .conception has not been achieved until reduction to practice has occurred", Amgen, Inc. v. Chugai Pharmaceutical Co, Ltd., 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991). Attention is also directed to the decision of The Regents of the University of California v. Eli Lilly and Company (CAFC, July 1997) wherein is stated:

"The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA." See Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1,2,9-32,34-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lobb et al. (US Patent 5,871,734) as evidenced by Arrhenius et al. (US Patent 5,869,448) in view of Schramm et al., Wigzell et al. (US Patent 5,958,410)

and Krause et al. (US Patent Application Publication 2002/0037286).

Lobb et al. teach use of antibody against VLA-4 to treat asthma (see abstract).

VLA-4 is a receptor on T cells (see Arrhenius et al., column 63, last paragraph). AHR occurs in asthma (see column 12, Example 2). Lobb et al. teach aerosol administration of antiVLA-4 antibody (see column 12, Example 2). Lobb et al. teach use of humanized antiVLA-4 antibody (see column 5, penultimate paragraph). Said antibody does not stimulate T cell activation (said antibodies inhibit VLA-4 function, see column 7, penultimate paragraph). Lobb et al. teach use of monovalent antibody (see column 7, third paragraph). Lobb et al. teach use of antibody dosages encompassed by those recited in claims 18 and 19 (see column 6, penultimate paragraph). Lobb et al. teach administration of said antibody in PBS via nebulized spray (see column 6, penultimate paragraph). Lobb et al. teach the method of claim 27 (see claim 17). Lobb et al. teach the method of claims 28,31,32 (see column 12, Example 2). *Lobb et al. teach that the effect seen can be achieved without detectable blood levels of antibody (see column 12, last paragraph) wherein the antibody would not therefore substantially effect peripheral immune function (eg. because it was not present in the blood)*. Lobb et al. teach use of said method in humans (see claim 16). Lobb et al. teach that their method resulted in a 70% decrease in inhibition of late phase response which would correlate with the improved FEV1 as per claim 34. Lobb et al. do not teach use of antiTCR $\alpha\beta$ antibodies. Schramm et al. teach use of IV antiTCR $\alpha\beta$ antibodies to treat asthma (see abstract). Krause et al. teach that antibodies which inhibit T cell activation are preferably administered via pulmonary aerosol (see section [0118] and abstract). Wigzell et al. teach that pathologic T cells found in the lungs can be treated via intrapulmonary (AKA pulmonary aerosol) administration of antiTCR antibody(see column 13, second paragraph and column 12, penultimate paragraph). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Lobb et al. teach aerosol administration of an antibody which binds T cells to treat asthma and Schramm et al. teach that a different antibody which binds T cells (antiTCR $\alpha\beta$) can be used to treat asthma. One of ordinary skill in the art would have been motivated to do the aforementioned because Lobb et al.

teach that the anti T cell antibody can be administered in a variety of art known routes including aerosol. One of ordinary skill in the art would have also been motivated to do the aforementioned because Krause et al. teach that antibodies which inhibit T cell activation are preferably administered via pulmonary aerosol (see section [0118] and abstract) and Wigzell et al. teach that pathologic T cells found in the lungs can be treated via intrapulmonary (AKA pulmonary aerosol) administration of antiTCR antibody(see column 13, second paragraph and column 12, penultimate paragraph). A neutralizing antibody would have been used in the claimed method because Schramm et al. teach that asthma symptoms are reduced in the absence of TCR$\alpha\beta$ T cells (see abstract). Regarding the particular dosages of formulation or dosage per weight, a routineer would initially test a wide variety of different dosages in order to have determined the smallest effective dose of the antibody used. A routineer would have administered said antibody in conjunction with art known treatments for asthma such as those disclosed in column 2, first paragraph of Lobb et al. The antibody would have been administered either before or during asthma symptoms.

Regarding claim 36 and newly amended claim 1, Lobb et al. teach that the effect seen can be achieved without detectable blood levels of antibody (see column 12, last paragraph) wherein the aerosol administered antibody would therefore not substantially effect peripheral immune T cell responses (eg. because it was not present in the blood). Regarding applicants comments, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Lobb et al. teach aerosol administration of an antibody which binds T cells to treat asthma and Schramm et al. teach that a different antibody which binds T cells (antiTCR $\alpha\beta$) can be used to treat asthma. In addition, Krause et al. teach that antibodies which inhibit T cell activation are preferably administered via pulmonary aerosol (see section [0118] and abstract) and Wigzell et al. teach that pathologic T cells found in the lungs can be treated via intrapulmonary (A.K.A. pulmonary aerosol) administration of antiTCR antibodies(see column 13, second paragraph and column 12, penultimate paragraph). Regarding applicants comments about motivation, Krause et al. teach that antibodies which inhibit T cell activation are preferably administered via pulmonary aerosol (see section [0118] and abstract) and Wigzell et al. teach that pathologic T cells found in the lungs can be treated via intrapulmonary (A.K.A.

pulmonary aerosol) administration (see column 13, second paragraph and column 12, penultimate paragraph). In addition, one of ordinary skill in the art would have been motivated to do the aforementioned because Lobb et al. teach that the anti T cell antibody can be administered in a variety of art known routes including aerosol.
Regarding applicants comments about Lobb et al., Schramm et al. teach that an antibody which binds T cells (antiTCR αβ) can be used to treat asthma. Thus, the art recognized that an antiTCR αβ could be used to treat asthma. Furthermore, Lobb et al. disclose:

"For instance, to the extent that the beneficial effects reported herein are due to the inhibition of leukocyte recruitment to VCAM-1 expressing endothelium..." (column 8, last paragraph).

Thus, Lobb et al. contemplate that their method involves inhibition of leukocytes including T cells. Lobb et al. teach use of antibody against VLA-4 to treat asthma (see abstract). VLA-4 is a receptor on T cells (see Arrhenius et al., column 63, last paragraph). Thus, the antibody taught by Lobb et al. binds T cells. Regarding applicants comments about Schramm et al., Schramm et al. teach use of IV antiTCR αβ antibodies to treat asthma (see abstract). Schramm et al. disclose that their results indicate that acute allergic responses are dependent on intact TCRαβ T cells. The animals have asthma, receive the antiTCR antibody and the asthma related responses are resolved. Thus, the asthma is treated. Furthermore, the only actual data provided in the specification involves mouse models. Thus, it is unclear as to why the mouse data provided by Schramm et al. is any less relevant than the mouse data provided by applicant. Furthermore, there is no teaching in Schramm et al. that a complete systemic depletion of an entire T cell subset from an animal is required in the antibody treated animals. Lobb et al. teach use of antibody dosages encompassed by those recited in claims 18 and 19 (see column 6, penultimate paragraph). Regarding the particular dosages of formulation or dosage per weight, a routineer would initially test a wide variety of different dosages in order to have determined the smallest effective dose of the antibody used.
Regarding the Wigzell et al. reference, said reference discloses use of cytotoxic antiTCR antibodies which deplete T cells (see column 14, lines 4-7). Wigzell et al. teach that **pathologic T cells found in the lungs** can be treated via intrapulmonary (A.K.A. pulmonary aerosol) administration (see column 13, second paragraph and column 12,

penultimate paragraph). Regarding applicants comments about evidence of the effectiveness of pulmonary administration, applicant is reminded that all art is deemed enabled in the absence of evidence to the contrary. The MPEP section 2121 discloses:

PRIOR ART IS PRESUMED TO BE OPERABLE/ ENABLING
When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. In re Sasse, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). See also MPEP § 716.07.

There is no evidence of record that the Wigzell et al. reference lacks enablement.
Krause et al. teach that antibodies which inhibit T cell activation are preferably administered via pulmonary aerosol (see section [0118] and abstract). Krause et al. teach:
"When antibodies are used therapeutically, a preferred route of administration is by pulmonary aerosol.".
This statement is not limited to a particular antibody taught by Krause et al. In addition, as per above, there is no evidence of record that the Krause et al. reference is not enabled.
AHR occurs in asthma (see column 12, Example 2). Lobb et al. teach aerosol administration of antiVLA-4 antibody (see column 12, Example 2). Lobb et al. teach use of humanized antiVLA-4 antibody (see column 5, penultimate paragraph). One of ordinary skill in the art would have been motivated to do the aforementioned because Lobb et al. teach that the anti T cell antibody can be administered in a variety of art known routes including aerosol. One of ordinary skill in the art would have also been motivated to do the aforementioned because Krause et al. teach that antibodies which inhibit T cell activation are preferably administered via pulmonary aerosol (see section [0118] and abstract) and Wigzell et al. teach that pathologic T cells found in the lungs can be treated via intrapulmonary (A.K.A. pulmonary aerosol) administration of antiTCR antibody(see column 13, second paragraph and column 12, penultimate paragraph).

Regarding applicants comments about Fahy et al., the comments in page 9 of said reference indicate that the reason that their antibody was not effective was because it was an antibody that bound a soluble antigen (IgE) present in large quantities in the vascular space wherein said IgE acted as a "sink of IgE". Fahy et al. hypothesize that the antibody might have been more immunogenic via the aerosol route, but the successful results of Lobb et al. would tend to disagree with this hypothesis. The issue of noncompliant patients is not germane to the instant discussion. The hypothesis that aerosolized antibody was not delivered in sufficient quantity to the lower airways seems unlikely as a potential problem for the claimed invention because the successful results of Lobb et al. would tend to disagree with this hypothesis. Therefore, the most likely explanation for the results found by Fahy et al. is that their antibody was not effective was because it was antibody that bound a soluble antigen (IgE) present in large quantities in the vascular space wherein said IgE acted as a "sink of IgE". The antibody used in the claimed invention does not bind a soluble antigen. The antibody used in the claimed invention binds alphabeta TCR found on the surface of T cells. There is no evidence of record that soluble TCR is found in large quantities in the vascular space wherein said TCR acted as a "sink". Therefore, the results of Fahy et al. are not germane to the claimed invention. Furthermore, Lobb et al. teach aerosol administration of an antibody which binds T cells to treat asthma. In addition, Krause et al. teach that antibodies which inhibit T cell activation are preferably administered via pulmonary aerosol (see section [0118] and abstract) and Wigzell et al. teach that pathologic T cells found in the lungs can be treated via intrapulmonary (AKA pulmonary aerosol) administration of antiTCR antibody. (see column 13, second paragraph and column 12, penultimate paragraph). Regarding reasonable expectation of success, Lobb et al. teach aerosol administration of an antibody which binds T cells to treat asthma and Schramm et al. teach that a different antibody which binds T cells (antiTCR $\alpha\beta$) can be used to treat asthma. Krause et al. teach that antibodies which inhibit T cell activation are preferably administered via pulmonary aerosol (see section [0118] and abstract) and Wigzell et al. teach that pathologic T cells found in the lungs can be treated via intrapulmonary (A.K.A. pulmonary aerosol) administration of antiTCR antibody(see column 13, second paragraph and column 12, penultimate paragraph). Schramm et al. has already demonstrated that antiTCR$\alpha\beta$ antibody can be used to treat asthma. Lobb et al. have already used pulmonary administration of antibodies which bind T cells to

treat asthma. Regarding applicants comments about low dosage, the only claims that recited a dosage are claims 18-23. The dosages of claims 18 and 19 are taught by Lobb et al. Thus, applicants comments regarding dosage are irrelevant to claims other than 20-23.

The claimed invention encompasses a method of treating humans, but there is no disclosure in the specification of evidence that the dosages used in claims 20-23 would have any effect in humans. Thus, to the extent that applicant is arguing unexpected results, the results disclosed in the specification are not commensurate with the scope of the claimed invention.

Regarding applicants comments about the cellular specificity of the antigen bound by the antiVLA-4 antibody, given that said antibody binds T cells and that the antibody used by Schramm et al. binds T cells (antiTCR ab) and can be used to treat asthma, it is reasonable to conclude that the method of Lobb et al. using aerosol administration could be practiced using the antibody used by Schramm et al. that binds T cells (antiTCR $\alpha\beta$). Regarding applicants comments about advantages of the claimed invention, Krause et al. teach that antibodies which inhibit T cell activation are preferably administered via pulmonary aerosol (see section [0118] and abstract) and Wigzell et al. teach that pathologic T cells found in the lungs can be treated via intrapulmonary (AKA pulmonary aerosol) administration of antiTCR antibodies(see column 13, second paragraph and column 12, penultimate paragraph). Regarding applicants comments about gamma/delta T cells, said species is not the elected species and is not currently under examination.

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached on Monday to Thursday from 7:30am to 6:00pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at 571 272 0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the

Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600